

<b>INFORMATION DISCLOSURE CITATION</b> Form PTO-1449 (Modified) <i>(Use several sheets if necessary)</i>	<b>ATTY. DOCKET NO.</b> 6510-096CIP3	<b>SERIAL NO.</b> Not Available
	<b>APPLICANT</b> Mahley et al.	
	<b>FILING DATE</b> Herewith	<b>GROUP</b> Unassigned

## U.S. PATENT DOCUMENTS

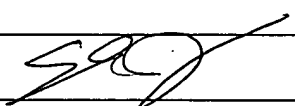
Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
SAD	AA	4,983,586	01/08/1991	Bodor			
	AB	5,002,935	03/26/1991	Bodor			
	AC	5,017,566	05/21/1991	Bodor			
SAD	AD	5,153,179	10/06/1992	Eibl			

## FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation
SAD	AE	WO 95/06470	03/09/1995	PCT			Yes No
	AF	WO 95/064565	03/09/1995	PCT			
SAD	AG	WO 94/13798	06/23/1994	PCT			

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

SAD	AH	Alberts, Mark J., et al., (1995) "ApoE Genotype and Survival from Intracerebral Haemorrhage", <i>The Lancet</i> 346:575.					
	AI	Beffert, U., et al., (1995) "Apolipoprotein E Uptake is Increased in the Presence of Beta Amyloid Peptides and Reduced by Blockade of the Low Density Lipoprotein Receptor", <i>Society for Neuroscience</i> 21:6					
	AJ	Baba et al. (1991) "Intracarotid infusion of leukotriene C4 selectively increases blood-brain barrier permeability after focal ischemia in rats." <i>J. Cereb. Blood Flow Metab.</i> , Vol. 11:638-643					
	AK	Battey et al. (1994) "The 39-kDa receptor-associated protein regulates ligand binding by the very low density lipoprotein receptor." <i>J. Biol. Chem.</i> , Vol. 269:23268-23273					
	AL	Bellosta et al. (1995) "Stable expression and secretion of apolipoproteins E3 and E4 in mouse neuroblastoma cells produces differential effects of neurite outgrowth." <i>J. Biol. Chem.</i> , Vol. 270:27063-27071					
	AM	Bickel et al. (1993) "Pharmacologic effects in vivo in brain by vector-mediated peptide drug delivery." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90:2618-2622					
	AN	Bilheimer et al. (1972) "The metabolism of very low density lipoproteins I. Preliminary in vitro and in vivo observations." <i>Biochem. Biophys. Acta.</i> , Vol. 260:212-221					
SAD	AO	Borth (1992) "α <sub>2</sub> -macroglobulin, a multifunctional binding protein with targeting characteristics." <i>FASEB J.</i> , Vol. 6:3345-3353.					

<b>EXAMINER</b> 	<b>DATE CONSIDERED</b> 12/6/90
<b>EXAMINER:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

35868 U.S. PTO

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		<b>APPLICANT</b> Mahley et al.	
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AP	Bottenstein et al. (1980) "Fibronectin and polylysine requirement for proliferation of neuroblastoma cells in defined medium." <i>Exp. Cell Res.</i> , Vol. 129:361-366
AQ	Boyles et al. (1985) "Apolipoprotein E associated with astrocytic glia of the central nervous system and with nonmyelinating glia of the peripheral nervous system." <i>J. Clin. Invest.</i> , Vol. 76:1501-1513.
AR	Boyles et al. (1989) "A role for apolipoprotein E, apolipoprotein A-1, and low density lipoprotein receptors in cholesterol transport." <i>J. Clin. Invest.</i> , Vol. 83:1015-1031.
AS	Chappell et al. (1993) "Lipoprotein lipase induces catabolism of normal triglyceride-rich lipoproteins via the low density lipoprotein receptor-related protein/ $\alpha_2$ -macroglobulin receptor in vitro." <i>J. Biol. Chem.</i> , Vol. 268:14168-14175
AT	Chen et al. (1988) "Calcium phosphate-mediated gene transfer: A highly efficient transfection system for stably transforming cells with plasmid DNA." <i>BioTechniques</i> , Vol. 6:632-638.
AU	Corder et al. (1993) "Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families." <i>Science</i> , Vol. 261:921-923.
AV	Crowther (1993) "Tau protein and paired helical filaments of Alzheimer's disease." <i>Curr. Opin. Struct. Biol.</i> , Vol. 3:202-206.
AW	Dong et al. (1994) "Human apolipoprotein E. Role of arginine 61 in mediating the lipoprotein preferences of the E3 and E4 isoforms." <i>J. Biol. Chem.</i> , Vol. 269:22358-22365.
AX	Dong et al. (1995) "Apolipoprotein E4 preference for very low density lipoproteins results from domain interaction mediated by glutamic acid-255 and arginine-61." <i>Circulation</i> , Vol. 92:1427-1428.
AY	Elshourbagy et al. (1985) "Apolipoprotein E mRNA is abundant in the brain and adrenals, as well as in the liver, and is present in other peripheral tissues of rats and marmosets." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 82:203-207.
AZ	Feskens et al. (1994) "Apolipoprotein e4 allele and cognitive decline in elderly men." <i>BMJ</i> , Vol. 309:1202-1206.
BA	Forss-Petter et al. (1990) "Transgenic mice expressing $\beta$ -galactosidase in mature neurons under neuron-specific enolase promoter control." <i>Neuron</i> , Vol. 5:187-197.
BB	Gennuso et al. (1993) "Effect of blood-brain barrier and blood-tumor barrier modification on central nervous system liposomal uptake." <i>Cancer Invest.</i> , Vol. 11:118-128.
BC	Godyna et al. (1995) "Identification of the low density lipoprotein receptor-related protein (LRP) as an endocytic receptor for thrombospondin-1." <i>J. Cell. Biol.</i> , Vol. 129:1403-1410.
BD	Goldstein et al. (1983) "Receptor-mediated endocytosis of low-density lipoprotein in cultured cells." <i>Met. Enzymol.</i> , Vol. 98:241-260
BE	Handelmann et al. (1992) "Effects of apolipoprotein E, $\beta$ -very low density lipoproteins, and cholesterol on the extension of neuritis by rabbit dorsal root ganglion neurons in vitro." <i>J. Lipid Res.</i> , Vol. 33:1677-1688.
BF	Helkala et al. (1995) "The association of apolipoprotein E polymorphism with memory: a population based study." <i>Neurosci. Letts.</i> , Vol. 191:141-144.
BG	Hoeg et al. (1987) "3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors in the treatment of hypercholesterolemia." <i>JAMA</i> , Vol. 258:3532-3536
BH	Holtzman et al. (1995) "LRP mediates apolipoprotein E-dependent neurite outgrowth in a CNS-derived neuronal cell line." <i>Soc. Neurosci.</i> , Vol. 21:1009

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SA	BI	Humphries et al. (1989) "Decreasing sulfation of proteoglycans produced by cultured cells." <i>Met. Enzymol.</i> , Vol. 179:428-434.	
	BJ	Hyman et al. " $\alpha_2$ -macroglobulin receptor/low density lipoprotein receptor-related protein." <i>Annals New York Academy of Sciences</i> , pgs. 88-95	
	BK	Ignatius et al. (1986) "Expression of apolipoprotein E during nerve degeneration and regeneration." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 83:1125-1129.	
	BL	Ignatius et al. (1987) "Lipoprotein uptake by neuronal growth cones in vitro." <i>Science</i> , Vol. 236:959-962.	
	BM	Innerarity et al. (1979) "Binding of arginine-rich (E) apoprotein after recombination with phospholipid vesicles to the low density lipoprotein receptors of fibroblasts." <i>J. Biol. Chem.</i> , Vol. 254:4186-4190.	
	BN	Innerarity et al. (1983) "The receptor-binding domain of human apolipoprotein E." <i>J. Biol. Chem.</i> , Vol. 258:12341-12347	
	BO	Jackowski, Andres, (1995) "Neural Injury Repair: Hope for the Future as Barriers to Effective CNS Regeneration Become Clearer", <i>British Journal of Neurosurgery</i> , 9:303-317.	
	BP	Ji et al. (1994) "Secretion-capture role for apolipoprotein E in remnant lipoprotein metabolism involving cell surface heparan sulfate proteoglycans." <i>J. Biol. Chem.</i> , Vol. 269:2764-2772.	
	BQ	Ji et al. (1994) "Lactoferrin binding to heparan sulfate proteoglycans and the LDL receptor-related protein." <i>Arterioscler. Thromb.</i> , Vol. 14:2025-2032.	
	BR	Ji et al. (1994) "Enhanced binding and uptake of remnant lipoproteins by hepatic lipase-secreting hepatoma cells in culture." <i>J. Biol. Chem.</i> , Vol. 269:13429-13436.	
	BS	Ji et al. (1993) "Role of heparan sulfate proteoglycans in the binding and uptake of apolipoprotein E-enriched remnant lipoproteins by cultured cells." <i>J. Biol. Chem.</i> , Vol. 268:10160-10167	
	BT	Kostis et al. (1994) "Central nervous system effects of HMG CoA reductase inhibitors: Lovastatin and pravastatin on sleep and cognitive performance in patients with hypercholesterolemia." <i>J. Clin. Pharmacol.</i> , Vol. 34:989-996	
	BU	Kounnas et al. (1992) "The $\alpha_2$ -macroglobulin receptor/low density lipoprotein receptor-related protein binds and internalizes pseudomonas exotoxin A." <i>J. Biol. Chem.</i> , Vol. 267:12420-12423.	
	BV	Kowal (1989) "Low density lipoprotein receptor-related protein mediates uptake of cholesteryl esters derived from apoprotein E-enriched lipoproteins." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 86:5810-5814.	
	BW	Lawn (1982) "Lipoprotein(a) in heart disease." <i>Scientific American</i> , pgs. 54-60	
	BX	Levin (1980) "Relationship of octanol/water partition coefficient and molecular weight in rat brain capillary permeability." <i>J. Med. Chem.</i> , Vol. 23:682-684.	
	BY	Lopes et al. (1994) "Expression of $\alpha_2$ -macroglobulin receptor/low density lipoprotein receptor-related protein is increased in reactive and neoplastic glial cells." <i>FEBS Lett.</i> , Vol. 338:301-305.	
SA	BZ	Ma, J., et al., (1995) "Promotion of the Neurotoxicity of Alzheimer A $\beta$ Protein by the Pathological Chaperones Act and ApoE4: Inhibition by A $\beta$ -Related Peptides and ApoE2", <i>Society for Neuroscience</i> 21:1714	

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SAC	CA	Mahley (1988) "Apolipoprotein E: Cholesterol transport protein with expanding role in cell biology." <i>Science</i> , Vol. 240:622-630.
	CB	Mahley "Apolipoprotein E: Structure and function in lipid metabolism and neurobiology." <i>The Molecular and Genetic Bases of Neurological Disease</i> , 2 <sup>nd</sup> ed., 41 pgs. Total
	CC	Mahley et al. (1994) "Role of heparan sulfate proteoglycans and the LDL receptor-related protein in remnant lipoprotein metabolism." <i>Ann. N.Y. Acad. Sci. USA</i> , Vol. 737:39-52.
	CD	Mahley et al. (1991) "Chylomicron and chylomicron remnant catabolism." <i>Curr. Opin. Lipidol.</i> , Vol. 2:170-176.
	CE	Mahley et al. (1987) "Canine hyperlipoproteinemia and atherosclerosis." <i>Am. J. Pathol.</i> , Vol. 87:205-226.
	CF	Mahley et al. "Apolipoprotein E: Structure, function, and possible roles in modulating neurite extension and cytoskeletal activity." <i>Research and Perspectives in Alzheimer's Disease</i> , pgs. 1-16
	CG	McKhann et al. (1984) "Clinical diagnosis of Alzheimer's disease." <i>Neurol.</i> , Vol. 34:939-944.
	CH	Medh et al. (1995) "The 39-kDa receptor-associated protein modulates lipoprotein catabolism by binding to LDL receptors." <i>J. Biol. Chem.</i> , Vol. 270:536-540
	CI	Meilinger et al. (1995) "Removal of lactoferrin from plasma is mediated by binding to low density lipoprotein receptor-related protein/ $\alpha_2$ macroglobulin receptor and transport to endosomes." <i>FEBS Lett.</i> , Vol. 360:70-74.
	CJ	Muller et al. (1985) "A specific 37,000-dalton protein that accumulates in regenerating but not in nonregenerating mammalian nerves." <i>Science</i> , Vol. 228:499-501.
	CK	Nathan et al. (1995) "The inhibitory effect of apolipoprotein E4 on neurite outgrowth is associated with microtubule depolymerization." <i>J. Biol. Chem.</i> , Vol. 270:19791-19799.
	CL	Nathan et al. (1994) "Differential effects of apolipoproteins E3 and E4 on neuronal growth in vitro." <i>Science</i> , Vol. 264:850-852.
	CM	Nathan et al. (1994) "The inhibition of neurite outgrowth by apolipoprotein E4 is mediated through the low density lipoprotein receptor-related protein." <i>Soc. Neurosci.</i> , Vol. 20(part 2):1033
	CN	Neuwelt et al. (1994) "Modification of the blood brain barrier in the chemotherapy of malignant brain tumors." <i>Fed. Proc.</i> , Vol. 43:214-219.
	CO	Orlando et al. (1994) "Functional domains of the receptor-associated protein (RAP)." <i>Proc. Natl Acad. Sci. USA</i> , Vol. 91:3161-3165
	CP	Orth et al. (1994) "Low density lipoprotein receptor-related protein is necessary for the internalization of both tissue-type plasminogen activator-inhibitor complexes and free tissue-type plasminogen activator." <i>J. Biol. Chem.</i> , Vol. 269:21117-21122.
	CQ	Pardridge (1992) "Recent developments in peptide drug delivery to the brain." <i>Pharmacol. Toxicol.</i> , Vol. 71:3-10
	CR	Pardridge (1994) "New approaches to drug delivery through the blood-brain barrier." <i>Tibtech</i> , Vol. 12:239-245
	CS	Petersen et al. (1995) "Apolipoprotein E status as a predictor of the development of Alzheimer's disease in memory-impaired individuals." <i>JAMA</i> , Vol. 273:1274-1278.
	CT	Pitas et al. (1987) "Astrocytes synthesize apolipoprotein E and metabolize apolipoprotein E-containing lipoproteins." <i>Biochem. Biophys. Acta</i> , Vol. 917:148-161.

<b>EXAMINER</b> SAC	<b>DATE CONSIDERED</b> 12/07/02
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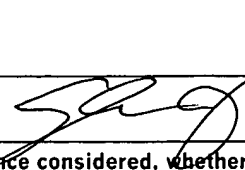
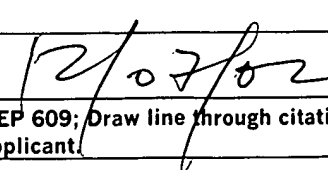
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<i>SAQ</i>	CU	Pitas et al. (1987) "Lipoproteins and their receptors in the central nervous system." <i>J. Biol. Chem.</i> , Vol. 262:14352-14360.	
	CV	Pitas et al. (1983) "Foam cells in explants of atherosclerotic rabbit aortas have receptors for $\beta$ -very low density lipoproteins and modified low density lipoproteins." <i>Arteriosclerosis</i> , Vol. 3:2-12.	
	CW	Pitas et al. (1981) "Acetoacetylated lipoproteins used to distinguish fibroblasts from macrophages in vitro by fluorescence microscopy." <i>Arteriosclerosis</i> , Vol. 1:177-185	
	CX	Pitas et al. (1980) "Cell surface receptor binding of phospholipid protein complexes containing different ratios of receptor-active and -inactive E apoprotein." <i>J. Biol. Chem.</i> , Vol. 255:5454-5460	
	CY	Pittman et al. (1987) "Synthetic high density lipoprotein particles." <i>J. Biol. Chem.</i> , Vol. 262:2435-2442.	
	CZ	Prudinger (1976) in "Peptide Hormones, ed. J.A. Parsons, University Park Press, Baltimore, pgs. 1-7.	
	DA	Quon et al. (1991) "Formation of $\beta$ -amyloid protein deposits in brains of transgenic mice." <i>Nature</i> , Vol. 352:239-241.	
	DB	Rebeck et al. (1995) "Multiple, diverse senile plaque-associated proteins are ligands of an apolipoprotein E receptor, the $\alpha_2$ -macroglobulin receptor-low density-lipoprotein receptor-related protein." <i>Annals of Neurology</i> , Vol. 37:211-217	
	DC	Reed et al. (1994) "Lower cognitive performance in normal older adult male twins carrying the apolipoprotein E $\epsilon 4$ allele." <i>Arch. Neurol.</i> , Vol. 51:1189-1192.	
	DD	Roheim et al. (1979) "Apolipoproteins in human cerebrospinal fluid." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 76:4646-4649	
	DE	Roses (1994) "The Alzheimer's diseases." <i>Curr. Neurol.</i> , Vol 14:111-141.	
	DF	Rudinger, J., (1976) "Characteristics of the Amino Acids as Components of a Peptide Hormone Sequence", <i>Peptide Hormones</i> ed. J.A. Parsons, University Park Press, Baltimore, pp. 1-7.	
	DG	Sambrook et al. (1989) <i>Molecular Cloning: A laboratory manual</i> , 2 <sup>nd</sup> ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.	
	DH	Saunders et al. (1993) "Association of apolipoprotein E allele $\epsilon 4$ with late-onset familial and sporadic Alzheimer's disease." <i>Neurol.</i> , Vol. 43:1467-1472.	
	DI	Selkoe (1991) "The molecular pathology of Alzheimer's disease." <i>Neuron</i> , Vol. 6:487-498.	
	DJ	Schneider et al. (1985) "Purification of the LDL receptor." <i>Met. Enzymol.</i> , Vol. 109:405-417.	
	DK	Slater et al. (1988) "Mechanism of action and biological profile of HMG CoA reductase inhibitors. A new therapeutic alternative." <i>Drugs</i> , Vol. 36(3):72-82	
	DL	Spooner et al. (1988) "The ionization and distribution behavior of oleic acid in chylomicrons and chylomicron-like mulsion particles and the influence of serum albumin." <i>J. Biol. Chem.</i> , Vol. 263:1444-1453	
	DM	Strickland et al. (1991) "Primary structure of $\alpha_2$ -macroglobulin receptor-associated protein." <i>J. Biol. Chem.</i> , Vol. 266:13364-13369.	
<i>SAQ</i>	DN	Strickland et al. (1995) "LDL receptor-related protein: a multiligand receptor for lipoprotein and proteinase catabolism." <i>FASEB J.</i> , Vol. 9:890-898	
EXAMINER		DATE CONSIDERED	
<i>SAQ</i>		<i>12/07/01</i>	
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590	DO	Strittmatter et al. (1994) "Hypothesis: Microtubule instability and paired helical filament formation in the Alzheimer disease brain are related to apolipoprotein E genotype." <i>Exp. Neurol.</i> , Vol. 125:163-171.	
	DP	Tikkanen et al. (1987) "Treatment of familial and non-familial hypercholesterolaemia: a review of HMG-CoA reductase inhibitors and probucol." <i>Eur. Heart. J.</i> , Vol. 8(E):97-101	
	DQ	Tuomanen (1993) "Breaching the blood-brain barrier." <i>Scientific American</i> , pgs. 80-84	
	DR	Warshawsky et al. (1993) "Identification of domains on the 39-kDa protein that inhibit the binding of ligands to the low density lipoprotein receptor-related protein." <i>J. Biol. Chem.</i> , Vol. 268:22046-22054.	
	DS	Warshawsky et al. (1995) "Sites within the 39-kDa protein important for regulating ligand binding to the low-density lipoprotein receptor-related protein." <i>Biochem.</i> , Vol. 34:3404-3415.	
	DT	Warshawsky et al. (1994) "Identification of domains on the 39-kDa protein that inhibit the binding of ligands to the low density lipoprotein receptor-related protein." <i>Ann. N.Y. Acad. Sci.</i> , pgs. 514-517.	
	DU	Weisgraber et al. "The role of apolipoprotein E in the nervous system." <i>Curr. Opin. Lipidol.</i> , Vol. 5:110-116.	
	DV	Weisgraber, Karl H., et al., (1994) "Lipoproteins, Neurobiology, and Alzheimer's Disease: Structure and Function of Apolipoprotein E", <i>Current Opinion in Structural Biology</i> 4:507-515.	
	DW	Willnow et al. (1994) "Genetic deficiency in low density lipoprotein receptor-related protein confers cellular resistance to pseudomonas exotoxin A." <i>J. Cell. Sci.</i> , Vol. 107:719-726.	
	DX	Willnow et al. (1994) "Molecular dissection of ligand binding sites on the low density lipoprotein receptor-related protein." <i>J. Biol. Chem.</i> , Vol. 269:15827-15832.	
	DY	Willnow et al. (1994) "Low density lipoprotein receptor-related protein and gp 330 bind similar ligands, including plasminogen activator-inhibitor complexes and lactoferrin, an inhibitor of chylomicron remnant clearance." <i>J. Biol. Chem.</i> , Vol. 267:26172-26180.	
	DZ	Willnow et al. (1995) "Functional expression of low density lipoprotein receptor-related protein is controlled by receptor-associated protein in vivo." <i>Proc. Natl. Acad. Sci.</i> , Vol. 92:4537-4541	
	EA	Wittmaack et al. (1995) "Localization and regulation of the human very low density lipoprotein/apolipoprotein-E receptor: Trophoblast expression predicts a role for the receptor in placental lipid transport." <i>Endocrinol.</i> , Vol. 136:340-348	
590	EB	Sigma Catalog, Biochemical and Organic Compounds for Research and Diagnostic Clinical Reagents, Sigma Chemical Co., St. Louis, pgs. 671,846,920.	

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		Filing Date	February 12, 2002
		First Named Inventor	MAHLEY
		Group Art Unit	1047 1647
		Examiner Name	To Be Assigned Nichols
		Attorney Docket Number	UCAL096CIP3

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Examiner Signature		Date Considered	12/07/02
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		Filing Date	February 12, 2002
		First Named Inventor	MAHLEY
		Group Art Unit	1041 JLT
		Examiner Name	To Be Assigned
Sheet 2 of 2	Attorney Docket Number	UCAL096CIP3	

**OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
SAG		MAHLEY, ROBERT, ET AL.: Apolipoprotein E: Impact of Cytoskeletal Stability in Neurons and the Relationship to Alzheimer's Disease", Current Option in Lipidology, Vol. 6, No. 2, 1995, Pages 86-91	
		NATHAN, BRITTO P, ET AL.: "The Inhibitory effect of apolipoprotein E4 on Neurite Outgrowth is Associated with Microtubule Depolymerization", Journal of Biological Chemistry", Vol. 270, No. 34, 1995, pages 19791-19799	
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Examiner Signature	<i>SAG</i>	Date Considered	12/07/02
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